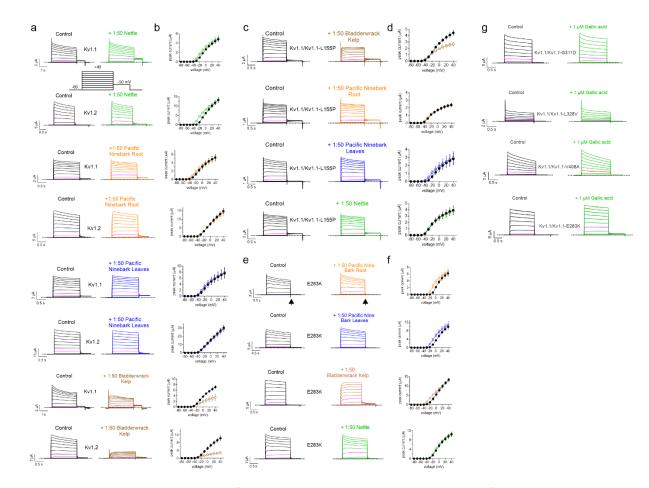


Supplementary Figure 1. Detection of gallic acid in F. gardneri and P. capitatus extracts.

Analysis of plant extracts after dilution 2- to 10-fold with MeOH was used to detect gallic acid by MS. In negative ionization mode authentic gallic acid showed molecular ion m/z 169 (M-H<sup>+</sup>) and daughter ion m/z 125. *F. gardneri* and *P. capitatus* (*leaves and roots*) gave solutions after dilution in MeOH and were directly injected onto the LC/MS. Gallic acid was identified in extract of *F. gardneri* and *P. capitatus* root.

Preparative RPHPLC of plant extracts (panels A-D). Aqueous plant extracts were diluted with 0.1% TFA/MeOH before injection. If 1:1 dilution didn't give solutions, additional 0.1% TFA/MeOH was added until a clear solution formed.

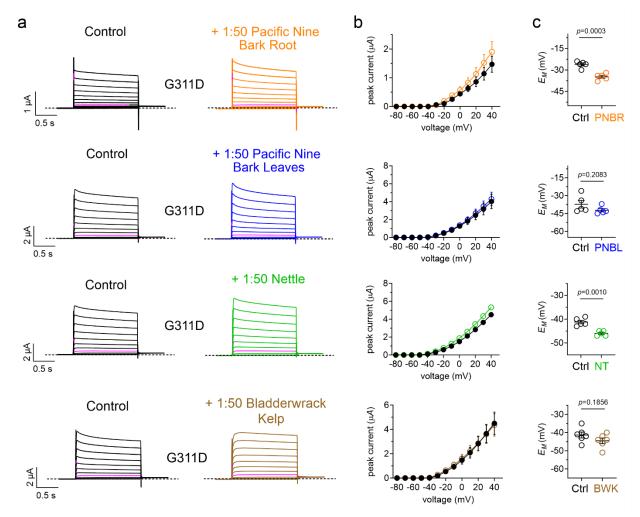
- a. Injection of authentic gallic acid (2.1 mg) in 0.1% TFA/MeOH with mobile phase 15 to 100% MeOH/water (both with 0.1% TFA) gave a single peak with retention time (RT) 1.4 min with UV maximum at 270 nm.
- b. Injection of *F. gardneri* extract (0.25 mL diluted with 0.75 mL 0.1% TFA/MeOH) showed peaks at 1.2 min, 1.35 min and a broad peak at RT 2.1 min. Analysis of the peak with RT 1.35 min after 10-fold dilution with MeOH showed the presence of gallic acid.
- c. The leaf extract of *P. capitatus* gave peaks with RT 1.2 and 1.4 min but LC/MS analysis did not show gallic acid.
- d. Injection of the *P. capitatus* root extract (0.5 mL diluted 1:1 with 0.1% TFA/MeOH) gave a major peak with RT 1.4 min that showed gallic acid by LC/MS after 10-fold dilution with MeOH.



#### Supplementary Figure 2. Full voltage families and IV plots to supplement main figures.

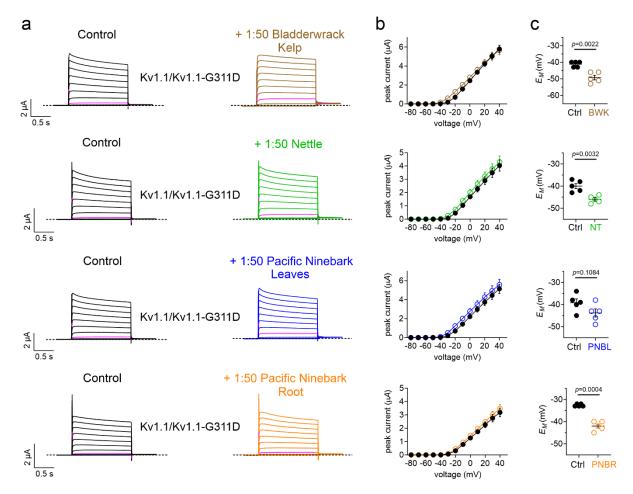
Voltage protocol as in Figure 2. Error bars indicate SEM. At least 2 batches of oocytes were used per experiment. Magenta traces indicate same-voltage traces within each pairing for ease of visual comparison.

- a, b. Full voltage families (a) and IV plots (b) for groups as in Figure 1b-d; Kv1.1 nettles (n = 5); Kv1.2 nettles (n = 6); Kv1.1 pacific ninebark root (n = 5); Kv1.2 pacific ninebark root (n = 5); Kv1.1 pacific ninebark leaves (n = 5); Kv1.2 pacific ninebark leaves (n = 5); Kv1.1 bladderwrack kelp (n = 4); Kv1.2 bladderwrack kelp (n = 6). Error bars indicate SEM.
- c, d. Full voltage families (c) and IV plots (d) for groups as in Figure 5b-d, n = 5. Error bars indicate SEM.
- e, f. Full voltage families (e) and IV plots (f) for groups as in Figure 6a-c, n = 5. Error bars indicate SEM.
- g. Full voltage families for groups as in Figure 7a-d, n = 5.



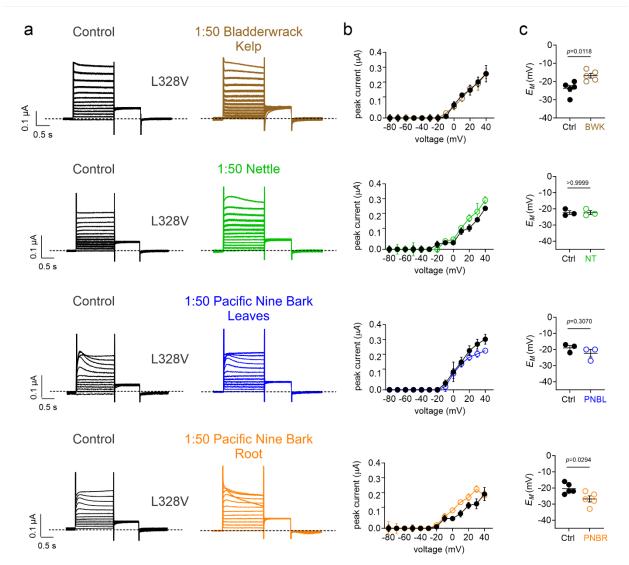
Supplementary Figure 3. Ataxia therapy extracts do not rescue the function of Kv1.1-G311D.

- a. Mean trace for Kv1.1-G311D in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean peak current versus voltage for Kv1.1-G311D traces as in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing Kv1.1-G311D in the absence (Control) and presence of plant extracts as in A; pacific ninebark root (n = 5; p = 0.0003); pacific ninebark leaves (n = 5; p = 0.2083); nettle (n = 5; p = 0.0010); bladderwrack kelp (n = 5; p = 0.1856).



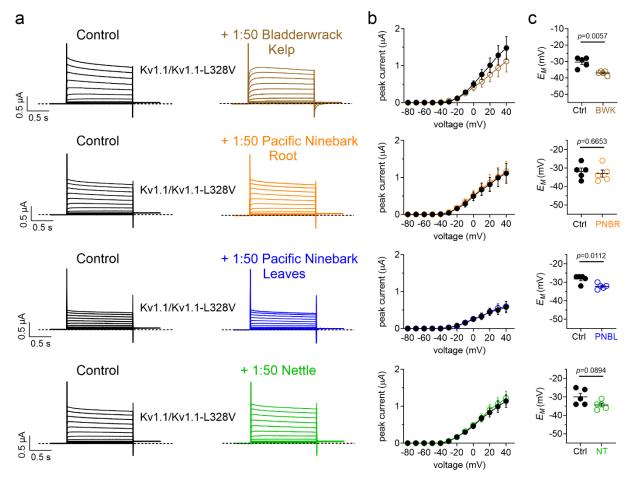
Supplementary Figure 4. Ataxia therapy extracts do not rescue the function of Kv1.1/Kv1.1-G311D.

- a. Mean trace for Kv1.1/Kv1.1-G311D in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean peak current versus voltage for Kv1.1/Kv1.1-G311D traces as in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing Kv1.1/Kv1.1-G311D in the absence (Control) and presence of plant extracts as in A; bladderwrack kelp (n = 5; p = 0.0022); nettle (n = 5; p = 0.0032); pacific ninebark leaves (n = 5; p = 0.1084); pacific ninebark root (n = 5; p = 0.0004).



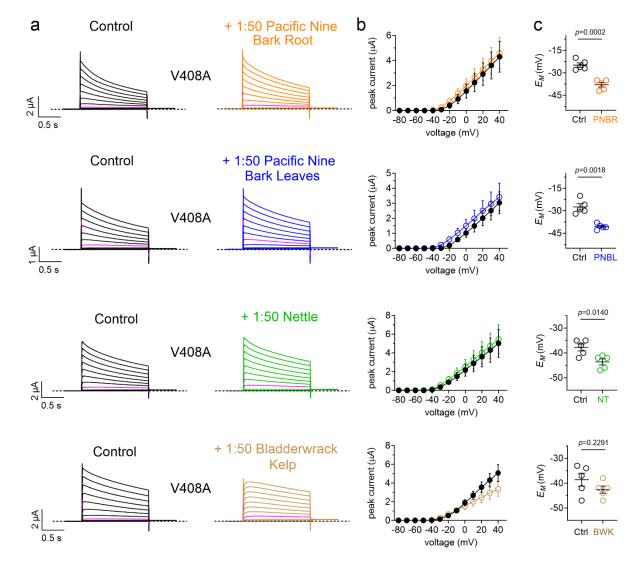
Supplementary Figure 5. Ataxia therapy plant extracts do not rescue the function of Kv1.1-L328V. Voltage protocol as in Figure 2. Error bars indicate SEM; statistical analysis by two-tailed paired t-test. At least 2 batches of oocytes were used per experiment. Magenta traces indicate same-voltage traces within each pairing for ease of visual comparison.

- a. Mean trace for Kv1.1-L328V in the absence (Control) and presence of plant extracts as indicated (1:50 dilution). bladderwrack kelp (n = 5); nettle (n = 3); pacific ninebark leaves (n = 3); pacific ninebark root (n = 5).
- b. Mean peak current versus voltage for Kv1.1-L328V traces in a; bladderwrack kelp (n = 5); nettle (n = 3); pacific ninebark leaves (n = 3); pacific ninebark root (n = 5).
- c. Mean  $E_M$  for oocytes expressing Kv1.1-L328V in the absence (Control) or presence of plant extracts as in a; bladderwrack kelp (n = 5; p=0.0118); nettle (n = 3; >0.9999); pacific ninebark leaves (n = 3; p=0.3070); pacific ninebark root (n = 5; p=0.0294).



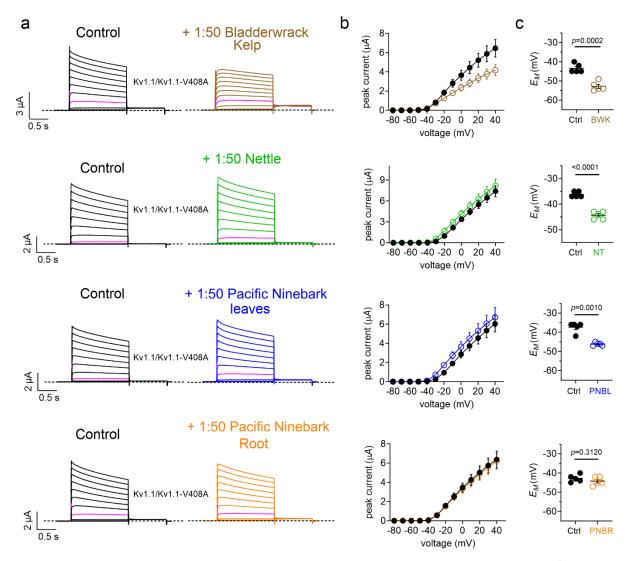
Supplementary Figure 6. Ataxia therapy plant extracts do not rescue the function of Kv1.1/Kv1.1-L328V.

- a. Mean trace for Kv1.1/Kv1.1-L328V in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean peak current versus voltage for Kv1.1/Kv1.1-L328V traces in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing Kv1.1/Kv1.1-L328V in the absence (Control) or presence of plant extracts as in a; bladderwrack kelp (n = 5; p = 0.0057); pacific ninebark root (n = 5; p = 0.6653); pacific ninebark leaves (n = 5; p = 0.0112); nettle (n = 5; p = 0.0894).



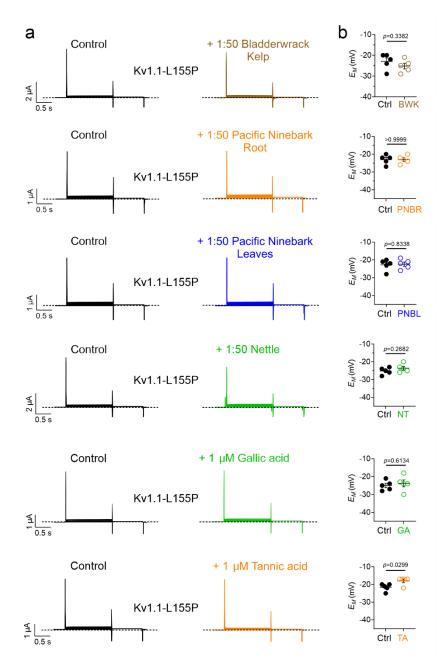
Supplementary Figure 7. Ataxia therapy plant extracts do not rescue the function of Kv1.1-V408A.

- a. Mean trace for Kv1.1-V408A in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean peak current versus voltage for Kv1.1-V408A traces in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing Kv1.1-V408A in the absence (Control) or presence of plant extracts as in a; pacific ninebark root (n = 5; p = 0.0002); pacific ninebark leaves (n = 5; p = 0.0018); nettle (n = 5; p = 0.0140); bladderwrack kelp (n = 5; p = 0.2291).



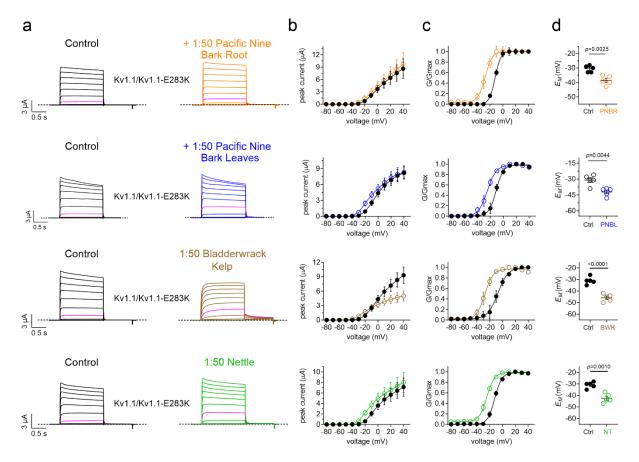
Supplementary Figure 8. Ataxia therapy plant extracts do not rescue the function of Kv1.1/Kv1.1-V408A.

- a. Mean trace for Kv1.1/Kv1.1-V408A in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean peak current versus voltage for Kv1.1/Kv1.1-V408A traces in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing Kv1.1/Kv1.1-V408A in the absence (Control) or presence of plant extracts as in a; bladderwrack kelp (n = 5; p=0.0002); nettle (n = 5; <0.0001); pacific ninebark leaves (n = 5; p=0.0010); pacific ninebark root (n = 5; p=0.3120).



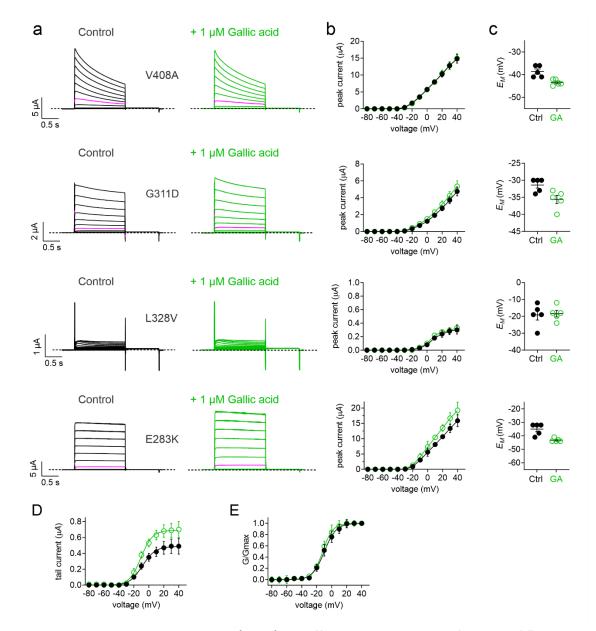
Supplementary Figure 9. Neither ataxia therapy plant extracts, nor gallic or tannic acids, rescue the function of "homozygous" Kv1.1-L155P.

- a. Mean trace for Kv1.1-L155P in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean  $E_{\rm M}$  for oocytes expressing Kv1.1-L155P in the absence (Control) or presence of plant extracts as in a; bladderwrack kelp (n=5; p=0.3382); pacific ninebark root (n=5; p=0.9999); pacific ninebark leaves (n=5; p=0.8338); nettle (n=5; p=0.2682); 1  $\mu$ M gallic acid (n=5; p=0.6134); 1  $\mu$ M tannic acid (n=5; p=0.0299).



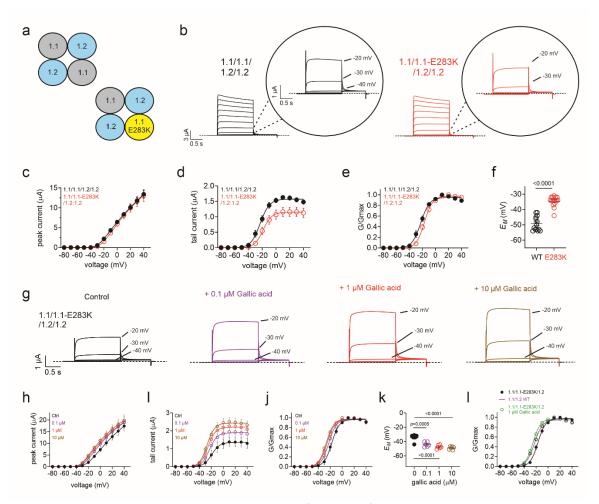
Supplementary Figure 10. Ataxia therapy plant extracts rescue the function of Kv1.1/Kv1.1-E283K.

- a. Mean trace for Kv1.1/Kv1.1-E283K in the absence (Control) and presence of plant extracts as indicated (1:50 dilution); n = 5.
- b. Mean peak current versus voltage for Kv1.1/Kv1.1-E283K traces in a; n = 5.
- c. Mean G/Gmax quantified from tail current for Kv1.1/Kv1.1-E283K traces as in a; n = 5.
- d. Mean  $E_{\rm M}$  for oocytes expressing Kv1.1/Kv1.1-E283K in the absence (Control) or presence of plant extracts as in a: pacific ninebark root (n = 5; p = 0.0025); pacific ninebark leaves (n = 5; p = 0.0044); bladderwrack kelp (n = 5; <0.0001); nettle (n = 5; p = 0.0010).



Supplementary Figure 11. Gallic acid (1  $\mu$ M) is ineffective at rescuing the function of "homozygous" Kv1.1 ataxia mutant channels.

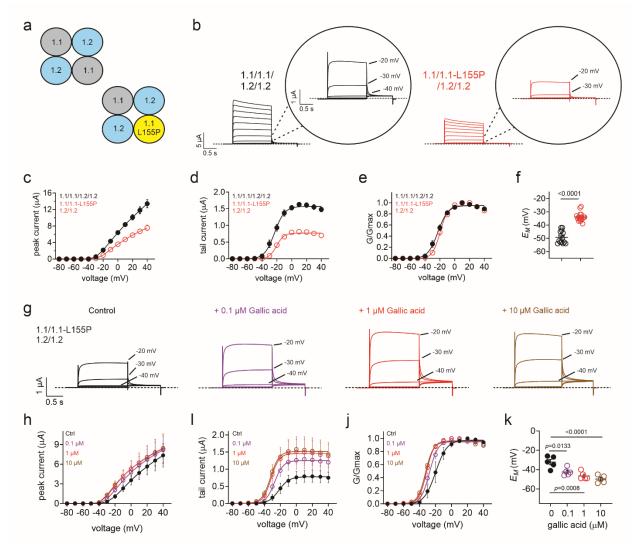
- a. Mean traces for ataxia mutant Kv1.1 channels as indicated in the absence (Control) and presence of gallic acid (1  $\mu$ M); n = 5.
- b. Mean peak current versus voltage for ataxia mutant Kv1.1 channels as in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing ataxia mutant Kv1.1 channels in the absence (Control) or presence of plant extracts as in a; Kv1.1-V408A (n = 5; p=0.0090); Kv1.1-G311D (n = 5; p=0.0248); Kv1.1-L328V (n = 5; p=0.8289); Kv1.1-E283K (n = 5; p=0.0101).
- d. Mean tail current versus voltage for Kv1.1-E283K channels as in a; n = 5.
- e. Mean G/Gmax versus voltage for Kv1.1-E283K channels as in a; n = 5.



Supplementary Figure 12. Gallic acid rescues the function of EA1-linked E283K heteromeric Kv1.1-Kv1.2 channels.

Voltage protocol as in Figure 2. Error bars indicate SEM; statistical analysis by two-tailed paired t-test or One-Way ANOVA. At least 2 batches of oocytes were used per experiment.

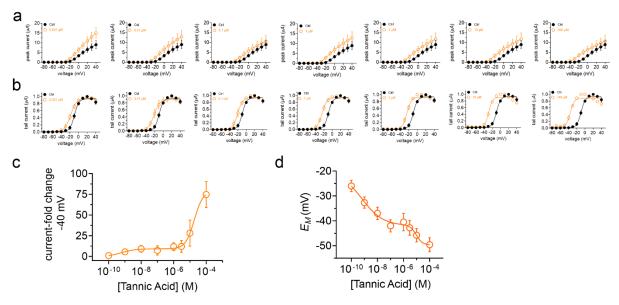
- a. cartoon representing the ratios of Kv1.x cRNA injected into each oocyte.
- b. Mean traces for heteromeric wild-type (left; n = 14) and E283K (right; n = 15) Kv1.1/Kv1.2 channels expressed in oocytes; scale bars lower left. Bubbles indicate vertical scale expanded region to show reduced current in mutant channels at mildly depolarized potentials.
- c-e. Mean peak, tail and normalized tail (G/Gmax) currents versus voltage for heteromeric wild-type (left; n = 14) and E283K (right; n = 15) Kv1.1/Kv1.2 channels.
- f. Mean  $E_{\rm M}$  for oocytes expressing heteromeric wild-type (left; n = 14) and E283K (right; n = 15) Kv1.1/Kv1.2 channels (<0.0001).
- g. Mean current traces for Kv1.1/Kv1.1-E283K/Kv1.2 channels in the absence or presence of gallic acid doses as indicated (n = 6).
- h-j. Mean peak, tail, and normalized (G/Gmax) currents versus voltage for channels as in g; n = 6.
- k. Mean  $E_{\rm M}$  for oocytes expressing Kv1.1/Kv1.1-E283K/Kv1.2 channels in; 0.1  $\mu$ M gallic acid (n = 6; p=0.0005); 1  $\mu$ M gallic acid (n = 6; <0.0001).
- I. Comparison of mean normalized tail currents (G/Gmax) showing that gallic acid (1  $\mu$ M) returns mutant E283K Kv1.1/Kv1.2 (n = 6) channel voltage dependence to match that heteromeric wild type (n = 14).



Supplementary Figure 13. Gallic acid rescues the function of EA1-linked L155P heteromeric Kv1.1-Kv1.2 channels.

Voltage protocol as in Figure 2. Error bars indicate SEM; statistical analysis by two-tailed paired t-test or One-Way ANOVA. At least 2 batches of oocytes were used per experiment.

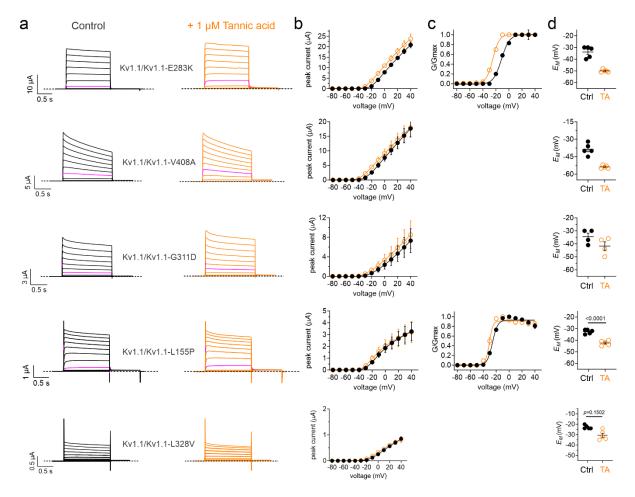
- a. cartoon representing the ratios of Kv1.x cRNA injected into each oocyte.
- b. Mean traces for heteromeric wild-type (left; n = 14) and L155P (right; n = 18) Kv1.1/Kv1.2 channels expressed in oocytes; scale bars lower left. Bubbles indicate vertical scale expanded region to show reduced current in mutant channels at mildly depolarized potentials.
- c-e. Mean peak, tail, and normalized tail (G/Gmax) currents versus voltage for heteromeric wild-type (left; n = 14) and L155P (right; n = 18) Kv1.1/Kv1.2 channels as in b.
- f. Mean  $E_{\rm M}$  for oocytes expressing heteromeric wild-type (left; n = 14) and L155P (right; n = 18) Kv1.1/Kv1.2 channels as in b (<0.0001).
- g. Mean current traces for Kv1.1/Kv1.1-L155P/Kv1.2 channels in the absence or presence of gallic acid doses as indicated (n = 5).
- h-j. Mean peak, tail, and normalized (G/Gmax) currents versus voltage for channels as in g; n = 5.
- k. Mean  $E_{\rm M}$  for oocytes expressing Kv1.1/Kv1.1-L155P/Kv1.2 channels in; 0.1  $\mu$ M gallic acid (n = 5; p=0.0133); 1  $\mu$ M gallic acid (n = 5; p=0.0008); 10  $\mu$ M gallic acid (n = 5; <0.0001).



Supplementary Figure 14. Dose response for tannic acid effects on Kv1.1-E283K.

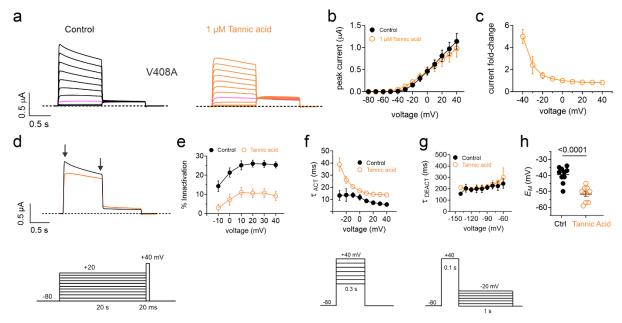
Voltage protocol as in Figure 2. Error bars indicate SEM. At least 2 batches of oocytes were used per experiment.

- a. Mean peak current versus voltage for Kv1.1-E283K in the absence (Control) or presence of tannic acid concentrations: 0.001  $\mu$ M (n = 4); 0.01  $\mu$ M (n = 4); 0.1  $\mu$ M (n = 6); 10  $\mu$ M (n = 6); 100  $\mu$ M (n = 6).
- b. Mean G/Gmax versus voltage for Kv1.1-E283K in the absence (Control) or presence of tannic acid concentrations as indicated: 0.001  $\mu$ M (n = 4); 0.01  $\mu$ M (n = 4); 0.1  $\mu$ M (n = 6); 1  $\mu$ M (n = 6); 100  $\mu$ M (n = 6).
- c. Dose response for tannic acid effects at -40 mV on Kv1.1-E283K calculated from graphs as in A. 0.001  $\mu$ M (n = 3); 0.01  $\mu$ M (n = 4); 0.1  $\mu$ M (n = 6); 1  $\mu$ M (n = 6); 10  $\mu$ M (n = 6).
- d. Dose response for tannic acid effects on  $E_{\rm M}$  of oocytes expressing Kv1.1-E283K, calculated from as in a: 0.001  $\mu$ M (n = 4); 0.01  $\mu$ M (n = 4); 0.1  $\mu$ M (n = 6); 1  $\mu$ M (n = 6); 10  $\mu$ M (n = 6).



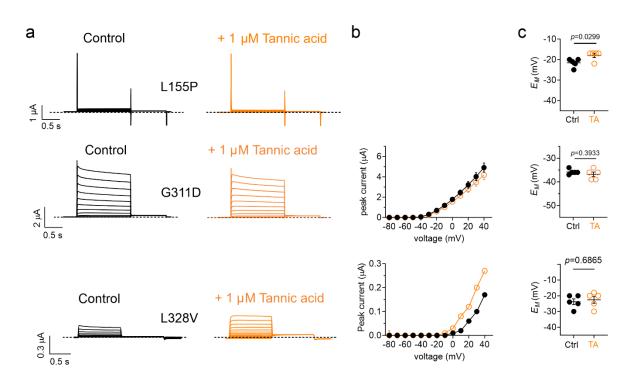
Supplementary Figure 15. Tannic acid (1  $\mu$ M) enhances Kv1.1/Kv1.1-E283K but no other mixed wild-type/ataxia mutant Kv1.1 channels.

- a. Mean trace for heteromeric channels as indicated in the absence (Control) and presence of tannic acid (1  $\mu$ M): Kv1.1/Kv1.1-E283K (n = 5); Kv1.1/Kv1.1-V408A (n = 5); Kv1.1/Kv1.1-G311D (n = 4); Kv1.1/Kv1.1-L155P (n = 5); Kv1.1/Kv1.1-L328V (n = 5).
- b. Mean peak currents versus voltage for traces as in a: Kv1.1/Kv1.1-E283K (n = 5); Kv1.1/Kv1.1-V408A (n = 5); Kv1.1/Kv1.1-G311D (n = 4); Kv1.1/Kv1.1-L155P (n = 5); Kv1.1/Kv1.1-L328V (n = 5).
- c. Mean G/Gmax versus voltage for traces as in a: Kv1.1/Kv1.1-E283K (n = 5); Kv1.1/Kv1.1-V408A (n = 5); Kv1.1/Kv1.1-G311D (n = 4); Kv1.1/Kv1.1-L155P (n = 5); Kv1.1/Kv1.1-L328V (n = 5). Graphs omitted where tail currents were too small to quantify.
- d. Mean  $E_{\rm M}$  for oocytes expressing channels as in a in the absence (Control) or presence of tannic acid (1  $\mu$ M) Kv1.1/Kv1.1-E283K (n = 5; p=0.0012); Kv1.1/Kv1.1-V408A (n = 5; p=0.0016); Kv1.1/Kv1.1-G311D (n = 4; p=0.1413); Kv1.1/Kv1.1-L155P (n = 5; <0.0001); Kv1.1/Kv1.1-L328V (n = 5; p=0.1502).



#### Supplementary Figure 16. Tannic acid (1 μM) effects on Kv1.1-V408A channels.

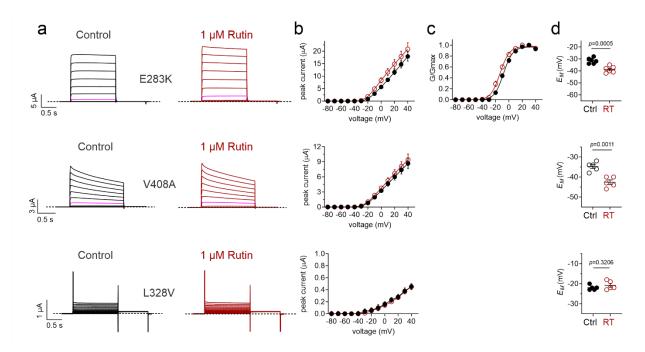
- a. Mean trace for homomeric Kv1.1-V408A channels in the absence (Control) and presence of tannic acid (1  $\mu$ M); n = 10; Voltage protocols as in Figure 2.
- b. Mean peak current versus voltage for traces as in a; n = 10.
- c. Current fold change induced by (1  $\mu$ M) tannic acid versus voltage for traces as in a; n = 10.
- d. Mean traces showing effects of tannic acid (1  $\mu$ M) on Kv1.1-V408A inactivation (between the two vertical bars) quantified using the voltage protocol shown (lower inset); n = 10.
- e. Effects of tannic acid (1  $\mu$ M) on % inactivation quantified as in d; n = 10.
- f. Mean activation rate ( $T_{ACT}$ ) versus voltage for Kv1.1-V408A in bath solution (black) versus tannic acid (1  $\mu$ M) (brown), quantified using the voltage protocol shown (lower inset); n = 10.
- g. Mean deactivation rate ( $T_{DEACT}$ ) versus voltage for Kv1.1-V408A in bath solution (black) versus tannic acid (1  $\mu$ M) (brown), quantified using the voltage protocol shown (lower inset); n = 8.
- h. Mean  $E_M$  for oocytes expressing channels as in a in the absence (Control) or presence of tannic acid (1  $\mu$ M); (n = 10; <0.0001).



Supplementary Figure 17. Tannic acid (1  $\mu$ M) does not rescue 100% mutant L155P, G311D or L328V Kv1.1 activity.

Voltage protocol as in Figure 2. Error bars indicate SEM; statistical analysis by two-tailed paired t-test. At least 2 batches of oocytes were used per experiment.

- a. Mean trace for channel as indicated in the absence (Control) and presence of tannic acid (1  $\mu$ M); n = 5.
- b. Mean peak current versus voltage for traces as in a; n = 5.
- c. Mean  $E_M$  for oocytes expressing channels as in a in the absence (Control) and presence Tannic acid (1  $\mu$ M): Kv1.1-L155P (n = 5; p = 0.0299); Kv1.1-G311D (n = 5; p = 0.3933); Kv1.1-L328V (n = 5; p = 0.6865).



# Supplementary Figure 18. Rutin (1 $\mu$ M) is ineffective at enhancing ataxia mutant Kv1.1 channel activity.

- a. Mean trace for channels as indicated in the absence (Control) and presence of rutin (1  $\mu$ M): Kv1.1-E283K (n = 6); Kv1.1-V408A (n = 5); Kv1.1-L328V (n = 5).
- b. Mean peak current versus voltage for traces as in a: Kv1.1-E283K (n = 6); Kv1.1-V408A (n = 5); Kv1.1-L328V (n = 5).
- c. Mean G/Gmax versus voltage for traces as in a: Kv1.1-E283K (n = 6); Kv1.1-V408A (n = 5); Kv1.1-L328V (n = 5). Graphs omitted where tail currents were too small to quantify.
- d. Mean  $E_M$  for oocytes expressing channels as in a in the absence (Control) and presence of rutin (1  $\mu$ M); Kv1.1-E283K (n = 6; p=0.0005); Kv1.1-V408A (n = 5; p=0.0011); Kv1.1-L328V (n = 5; p=0.3206).

## Supplementary Data – values and statistics tabulated by figure number.

Figure 1

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	E <sub>M</sub> (mV)
Control	-27.13 ± 1.47	5.56 ± 1.47	-39.80 ± 1.73
1:50 Nettle	-42.46 ± 1.94	7.46 ± 1.69 ( <i>p</i> =0.4214;	-45.40 ± 1.23
	( <i>p</i> =0.0003; n=5)	n=5)	( <i>p</i> =0.0211; n=5)

Statistics versus Kv1.1 in absence of Nettle. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-26.02 ± 1.15	5.93 ± 0.98	-41.20 ± 1.40
1:50 Pacific Ninebark	-38.85 ± 1.31 (<0.0001;	4.48 ± 1.25 ( <i>p</i> =0.3895;	-51.80 ± 1.97
Root	n=5)	n=5)	( <i>p</i> =0.0028; n=5)

Statistics versus Kv1.1 in absence of Pacific Ninebark Root. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-25.42 ± 1.29	6.45 ± 1.12	-47.40 ± 2.00
1:50 Pacific Ninebark	-36.56 ± 1.19	6.39 ± 1.04 ( <i>p</i> =0.9590;	-53.60 ± 1.34
Leaves	( <i>p</i> =0.0002; n=5)	n=5)	( <i>p</i> =0.0201; n=5)

Statistics versus Kv1.1 in absence of Pacific Ninebark Leaves. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-24.39 ± 0.77	6.76 ± 0.67	-36.80 ± 1.36
1:50 Bladderwrack Kelp	-41.82 ± 1.02 (<0.0001;	3.30 ± 1.04 ( <i>p</i> =0.0273;	-44.80 ± 1.34
	n=5)	n=5)	( <i>p</i> =0.0097; n=5)

Statistics versus Kv1.1 in absence of Bladderwrack Kelp. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-16.86 ± 0.38	4.97 ± 0.33	-30.50 ± 1.41
1:50 Nettle	-30.23 ± 0.71 (<0.0001;	4.36 ± 0.71 ( <i>p</i> =0.4673;	-44.67 ± 2.41
	n=5)	n=5)	( <i>p</i> =0.0007; n=5)

Statistics versus Kv1.2 in absence of Nettle. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>м</sub></i> (mV)
Control	-25.04 ± 0.45	6.45 ± 0.39	-39.60 ± 1.56
1:50 Pacific Ninebark	-27.28 ± 0.58	6.13 ± 0.50 ( <i>p</i> =0.6282;	-42.60 ± 0.61
Root	( <i>p</i> =0.0170; n=5)	n=5)	( <i>p</i> =0.0915; n=5)

Statistics versus Kv1.2 in absence of Pacific Ninebark Root. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-28.60 ± 0.40	7.46 ± 0.35	-48.00 ± 2.05
1:50 Pacific Ninebark	-28.31 ± 0.46	7.17 ± 0.41 ( <i>p</i> =0.6056;	-46.20 ± 1.80
Leaves	( <i>p</i> =0.6472; n=5)	n=5)	( <i>p</i> =0.4156; n=5)

Statistics versus Kv1.2 in absence of Pacific Ninebark Leaves. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-19.95± 0.83	6.40 ± 0.73	-33.67 ± 1.20
1:50 Bladderwrack Kelp	-34.48 ± 2.13	6.86 ± 1.86 (p=0.83;	-48.67 ± 0.7 (p=0.0009;
	( <i>p</i> =0.0005; n=6)	n=6)	n=6)

Statistics versus Kv1.2 in absence of Bladderwrack Kelp. Values indicate mean ± SEM.

Figure 2

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-11.67 ± 0.96	6.56 ± 0.84	-29.33 ± 1.92
100 μM Catechin	-14.70 ± 0.44	5.83 ± 0.38 ( <i>p</i> =0.4549;	-31.33 ± 2.31
Hydrate	( <i>p</i> =0.0242; n=6)	n=6)	( <i>p</i> =0.3238; n=6)

Statistics versus Kv1.1 in absence of catechin hydrate. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-11.55 ± 1.55	9.57 ± 1.40	-36.20 ± 0.78
100 μM Gallic acid	-37.17 ± 2.59 (<0.0001;	12.10 ± 2.32 ( <i>p</i> =0.3835;	-49.60 ± 0.91
	n=5)	n=5)	(p=0.0002; n=5)

Statistics versus Kv1.1 in absence of Gallic acid. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-22.35 ± 0.42	6.25 ± 0.56	-40.00 ± 2.53
100 μM Cytisine	-23.96 ± 1.37	8.15 ± 1.31 ( <i>p</i> =0.2357;	-41.60 ± 1.77
	( <i>p</i> =0.3148; n=5)	n=5)	( <i>p</i> =0.3949; n=5)

Statistics versus Kv1.1 in absence of Cytisine. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>м</sub></i> (mV)
Control	-21.99 ± 0.91	9.43 ± 0.92	-45.75 ± 1.20
100 μM Kaempferol	-22.40 ± 0.84	8.68 ± 0.87 ( <i>p</i> =0.5700;	-45.25 ± 1.83
	( <i>p</i> =0.8458; n=5)	n=5)	( <i>p</i> =0.6997; n=5)

Statistics versus Kv1.1 in absence of Kaempferol. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-25.70 ± 1.83	6.61 ± 1.10	-43.75 ± 3.30
100 μM Quercetin	-25.12 ± 1.81	6.00 ± 1.06 (>0.9999;	-43.50 ± 1.46
	(p=0.8292; n=4)	n=4)	(p=0.9438; n=4)

Statistics versus Kv1.1 in absence of Quercetin. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-22.70 ± 1.29	8.58 ± 1.28	-44.50 ± 1.73
100 μM Rutin	-31.59 ± 3.22	11.79 ± 2.88 (p=0.3642;	-56.75 ± 0.28
	( <i>p</i> =0.0634; n=4)	n=4)	( <i>p</i> =0.0065; n=4)

Statistics versus Kv1.1 in absence of Rutin. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail	Slope (mV)	$E_{M}$ (mV)
	current (mV)		
Control	-23.92 ± 1.01	8.41 ± 0.89	-38.40 ± 1.50
100 μM Tannic acid	-44.95 ± 2.49	13.67 ± 2.01 ( <i>p</i> =0.0575;	-54.40 ± 1.23 (<0.0001;
	(p=0.0004; n=5)	n=5)	n=5)

Statistics versus Kv1.1 in absence of Tannic acid. Values indicate mean ± SEM.

## Figure 3

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>м</sub></i> (mV)
Control	-21.91 ± 1.77	12.21 ± 1.58	-41.40 ± 1.00
1:50 Wild Oak Bark	-38.27 ± 1.73	10.44 ± 1.53 (p=0.4442;	-53.40 ± 0.63 (<0.0001;
	( <i>p</i> =0.0002; n=5)	n=5)	n=5)

Statistics versus Kv1.1 in absence of White Oak Bark. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-22.59 ± 1.76	11.34 ± 1.56	-45.40 ± 1.20
1:50 Cramp Bark	-35.31 ± 1.14	10.69 ± 0.74 (p=0.8283;	-48.20 ± 1.77
	(p=0.0006; n=5)	n=5)	( <i>p</i> =0.4146; n=5)

Statistics versus Kv1.1 in absence of Cramp Bark. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-22.19 ± 3.57	17.40 ± 3.49	-49.00 ± 1.32
1:50 Wild Cherry Bark	-36.46 ± 1.19	11.43 ± 1.06 ( <i>p</i> =0.1659;	-58.40 ± 0.97
	( <i>p</i> =0.0133; n=5)	n=5)	( <i>p</i> =0.0346; n=5)

Statistics versus Kv1.1 in absence of Wild Cherry Bark. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-21.46 ± 2.60	11.75 ± 2.31	-45.50 ± 0.91
1:50 White Willow Bark	-36.28 ± 0.83	10.69 ± 0.74 (p=0.6810;	-57.40 ± 0.20 (<0.0001;
	(p=0.0032; n=5)	n=5)	n=5)

Statistics versus Kv1.1 in absence of White Willow Bark. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-28.46 ± 1.36	8.47 ± 1.04	-48.33 ± 0.26
1:50 Sophora Japonica	-45.86 ± 2.43	8.31 ± 2.04 ( <i>p</i> =0.1863;	-65.83 ± 2.29
	( <i>p</i> =0.0430; n=6)	n=6)	( <i>p</i> =0.0002; n=6)

Statistics versus Kv1.1 in absence of *Sophora Japonica*. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>м</sub></i> (mV)
Control	-19.83 ± 0.65	7.93 ± 0.51	-35.12 ± 3.20
100 μM Oxymatrine	-21.86 ± 0.64 (p=xxx;	8.73 ± 0.24 ( <i>p</i> =xxx;	-39.88 ± 2.34
	n=8)	n=8)	(p=0.1720; n=8)

Statistics versus Kv1.1 in absence of Oxymatrine. Values indicate mean ± SEM.

#### Figure 4

KV1.1	EC50 (nM)
Tannic acid	136 ± 30 (n=7-12)
Gallic acid	379 ± 28 (n=5)
Rutin	363 ± 98 (n=5)

Kv1.1 dose responses for tannic acid, gallic acid, and rutin. Values indicate mean ± SEM.

KV1.2	EC50 (nM)
Tannic acid	222 ± 45 (n=5)
Gallic acid	<i>n.a</i> (n=5)
Rutin	855 ± 96 (n=5)

Kv1.2 dose responses for tannic acid, gallic acid, and rutin. Values indicate mean  $\pm$  SEM. n.a = not applicable.

Figure 5

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-31.61 ± 1.35	5.87 ± 1.19	-43.00 ± 0.97
1:50 Bladderwrack Kelp	-46.71 ± 2.07	3.99 ± 1.63 ( <i>p</i> =0.3813;	-54.40 ± 0.84 (<0.0001;
	( <i>p</i> =0.0005; n=5)	n=5)	n=5)

Statistics versus KV1.1/KV1.1-L155P in absence of Bladderwrack Kelp. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	-35.76 ± 0.92	5.88 ± 0.79	-45.80 ± 0.76
1:50 Pacific Ninebark	-40.80 ± 0.98	5.23 ± 0.90 ( <i>p</i> =0.6023;	-48.80 ± 1.23
Root	( <i>p</i> =0.0057; n=5)	n=5)	( <i>p</i> =0.0046; n=5)

Statistics versus KV1.1/KV1.1-L155P in absence of Pacific Ninebark Root. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail	Slope (mV)	$E_{M}$ (mV)
	current (mV)		
Control	-22.20 ± 0.62	4.76 ± 0.55	-38.40 ± 0.31
1:50 Pacific Ninebark	-32.30 ± 0.90 (<0.0001;	6.48 ± 0.78 ( <i>p</i> =1134;	-48.00 ± 0.23
Leaves	n=5)	n=5)	(p=0.0036; n=5)

Statistics versus KV1.1/KV1.1-L155P in absence of Pacific Ninebark Leaves. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-36.99 ± 0.41	5.00 ± 0.35	-46.20 ± 0.68
1:50 Nettle	-39.21 ± 0.55	3.88 ± 0.60 ( <i>p</i> =0.1546;	-49.00 ± 0.20
	(p=0.0133; n=5)	n=5)	( <i>p</i> =0.0348; n=5)

Statistics versus KV1.1/KV1.1-L155P in absence of Nettle. Values indicate mean ± SEM.

### Figure 6

	V <sub>0.5</sub> Normalized tail	Slope (mV)	$E_{M}$ (mV)
	current (mV)		
Control	-11.63 ± 1.11 (n=5)	7.55 ± 2.83 (n=5)	-30.80 ± 0.43
1:50 Bladderwrack Kelp	-29.20 ± 0.65 (<0.0001;	6.52 ± 0.80 ( <i>p</i> =0.7415;	-47.80 ± 0.84
	n=5)	n=5)	( <i>p</i> =0.0025; n=5)

Statistics versus Kv1.1-E283K in absence of bladderwrack kelp. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>м</sub></i> (mV)
Control	-4.98 ± 0.47 (n=5)	4.14 ± 1.59 (n=5)	-22.00 ± 0.28
1:50 Pacific Ninebark	-19.24 ± 0.87 (<0.0001;	3.27 ± 1.63 ( <i>p</i> =0.7124;	-34.20 ± 0.85
Root	n=5)	n=5)	( <i>p</i> =0.0009; n=5)

Statistics versus Kv1.1-E283K in absence of Pacific Ninebark root. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	E <sub>M</sub> (mV)
Control	-7.80 ± 1.03 (n=5)	7.03 ± 3.93 (n=5)	-24.80 ± 1.24
1:50 Pacific Ninebark	-19.88 ± 0.76 (<0.0001;	6.05 ± 2.81 ( <i>p</i> =0.8448;	-35.00 ± 0.84
Leaves	n=5)	n=5)	( <i>p</i> =0.0003; n=5)

Statistics versus Kv1.1-E283K in absence of Pacific Ninebark Leaves. Values indicate mean ± SEM.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>м</sub></i> (mV)
Control	-5.84 ± 1.09 (n=6)	6.18 ± 0.95 (n=6)	-35.40 ± 0.74
1:50 Nettle	-24.17 ± 0.55 (<0.0001;	5.00 ± 0.47 (p=0.2268;	-47.00 ± 0.83 (<0.0001;
	n=6)	n=6)	n=6)

Statistics versus Kv1.1-E283K in absence of Nettles. Values indicate mean ± SEM.

	Control Tau <sub>Act</sub> (ms)	1 μM Tannic acid
		Tau <sub>Act</sub> (ms)
-20 mV	19.99 ± 7.47	41.32 ± 8.47
		(p=0.0962; n=5)
-10 mV	10.66 ± 4.72	27.06 ± 7.08
		(p=0.0955; n=5)
0 mV	8.72 ± 4.64	21.12 ± 4.35
		(p=0.0872; n=5)
+10 mV	4.26 ± 1.26	17.43 ± 3.97
		(p=0.0265; n=5)
+20 mV	3.86 ± 1.20	12.72 ± 2.85
		(p=0.0324; n=5)
+30 mV	3.40 ± 1.06	10.63 ± 2.79
		(p=0.0587; n=5)
+40 mV	3.09 ± 0.91	10.04 ± 2.65
		(p=0.0565; n=5)

Statistics versus Kv1.1-E283K in absence of bladderwrack kelp. Values indicate mean ± SEM.

	Control Tau <sub>Deact</sub> (ms)	1 μM Tannic acid Tau <sub>Deact</sub> (ms)
-80 mV	0.88 ± 0.32	1.50 ± 0.57
		(p=0.3632; n=8)
-70 mV	0.38 ± 0.15	1.38 ± 0.56
		(p=0.1228; n=8)
-60 mV	0.32 ± 0.09	1.23 ± 0.52
		(p=0.1259; n=8)
-50 mV	0.20 ± 0.05	1.04 ± 0.44
		(p=0.0986; n=8)
-40 mV	0.19 ± 0.05	0.88 ± 0.36
		(p=0.0979; n=8)
-30 mV	0.19 ± 0.05	0.79 ± 0.32
		(p=0.1044; n=8)
-20 mV	0.19 ± 0.06	0.87 ± 0.36
		(p=0.1025; n=8)

Statistics versus Kv1.1-E283K in absence of bladderwrack kelp. Values indicate mean ± SEM.

Figure 7

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	n.a	n.a	-41.20 ± 1.84
1 μM Gallic acid	n.a	n.a	-47.00 ± 2.56
			( <i>p</i> =0.1067; n=5)

Statistics versus Kv1.1/Kv1.1-G311D in absence of Gallic acid. Values indicate mean  $\pm$  SEM. n.a = not applicable.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>E<sub>M</sub></i> (mV)
Control	n.a	n.a	-25.40 ± 1.37
1 μM Gallic acid	n.a	n.a	-33.00 ± 1.09
			( <i>p</i> =0.0131; n=5)

Statistics versus Kv1.1/Kv1.1-L328V in absence of Gallic acid. Values indicate mean  $\pm$  SEM. n.a = not applicable.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	n.a	n.a	-41.40 ± 1.98
1 μM Gallic acid	n.a	n.a	-46.60 ± 0.60
			( <i>p</i> =0.0289; n=5)

Statistics versus Kv1.1/Kv1.1-V408A in absence of Gallic acid. Values indicate mean  $\pm$  SEM. n.a = not applicable.

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	<i>Е<sub>м</sub></i> (mV)
Control	-12.01 ± 0.57	4.52 ± 0.51	-33.80 ± 0.18
1 μM Gallic acid	-27.50 ± 0.51 (<0.0001;	5.70 ± 1.12 ( <i>p</i> =0.3772;	-47.80 ± 0.65
	n=4)	n=4)	(p=0.0005; n=4)

Statistics versus Kv1.1/Kv1.1-E283K in absence of Gallic acid. Values indicate mean  $\pm$  SEM.

Figure 8

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	E <sub>M</sub> (mV)
Control	-23.84 ± 0.45	4.30 ± 0.35	-34.89 ± 0.98 (n=9)
1 μM Gallic acid	-30.59 ± 0.60 (<0.0001;	4.84 ± 0.56 ( <i>p</i> =0.4278;	-45.00 ± 0.78
	n=9)	n=9)	( <i>p</i> =0.0002; n=9)
10 μM Gallic acid	-36.38 ± 0.62 (<0.0001;	4.76 ± 0.51 ( <i>p</i> =0.4692;	-48.89 ± 0.66 (<0.0001;
	n=9)	n=9)	n=9)
100 μM Gallic acid	-37.93 ± 0.62 (<0.0001;	4.68 ± 0.55 ( <i>p</i> =0.5695;	-50.11 ± 0.69 (<0.0001;
	n=9)	n=9)	n=9)

Statistics versus Kv1.1/Kv1.1-L155P in absence of Gallic acid. Values indicate mean ± SEM.

Figure 9

	V <sub>0.5</sub> Normalized tail current (mV)	Slope (mV)	E <sub>M</sub> (mV)	Current-fold change -30 mV
Control	-11.21 ± 0.61	5.13 ± 0.60	-27.00 ± 0.35	n.a
1 μM Tannic acid	-22.75 ± 1.34	8.70 ± 1.19	-44.83 ± 0.14	4.69 ± 1.69
	(<0.0001; n=6)	(p=0.0301; n=6)	(<0.0001; n=6)	(<0.0001; n=6)

Statistics versus Kv1.1-E283K in absence of Tannic acid. Values indicate mean  $\pm$  SEM. n.a = not applicable.

_	Control Tau <sub>Act</sub> (ms)	1 μM Tannic acid
		Tau <sub>Act</sub> (ms)
-20 mV	24.46 ± 3.97	31.31 ± 2.98
		(p=0.2679; n=6)
-10 mV	15.41 ± 2.70	20.71 ± 2.35
		(p=0.1701; n=6)
0 mV	11.02 ± 1.62	15.70 ± 1.40
		(p=0.0543; n=6)
+10 mV	8.90 ± 0.89	12.94 ± 1.05
		(p=0.0153; n=6)
+20 mV	7.43 ± 0.68	11.30 ± 0.89
		(p=0.0068; n=6)
+30 mV	6.35 ± 0.66	10.16 ± 0.83
		(p=0.0053; n=6)
+40 mV	5.50 ± 0.69	9.46 ± 0.83
		(p=0.0046; n=6)

Statistics versus Kv1.1-E283K in absence of Tannic acid. Values indicate mean ± SEM.

	Peak current at -40 mV (μA)
Control	0.02 ± 0.01
0.1 μΜ	0.02 ± 0.01
	(>0.9999; n=5)
1 μΜ	0.02 ± 0.01
	(>0.9999; n=5)
10 μΜ	0.02 ± 0.01
	(>0.9999; n=5)
30 μΜ	0.02 ± 0.01
	(>0.9999; n=5)
100 μΜ	0.03 ± 0.01
	( <i>p</i> =0.496; n=5)

Statistics versus Kv1.1-E283K in absence of Tannic acid. Values indicate mean ± SEM.

Figure 10

	EC50 (nM)
Kv1.1	379 ± 28 (n=5)
Kv1.1-3M	n.a

Kv1.1 vs Kv1.1-3M dose responses for gallic acid. Values indicate mean  $\pm$  SEM. n.a = not applicable.

	EC50 (nM)
Kv1.1	18 ± 6 (n=5)
Kv1.1-3M	345 ± 38 (n=5)

Kv1.1 vs Kv1.1-3M resting membrane potential ( $E_M$ ) dose responses for gallic acid. Values indicate mean  $\pm$  SEM.